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Note

Benzopyrans : Part 36†—A simple synthesis of 3-hydroxymethylchromone

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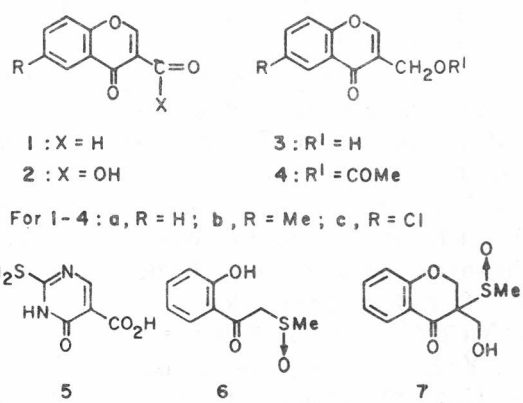
The aldehyde **1** is reduced to the alcohol **3** by diborane but the acid **2** remains unaffected.

We needed the title chromone **3** in connection with some synthetic work and explored the possibility for its formation from the easily accessible either the corresponding aldehyde **1**[1,2] or the acid **2**[2,3]. 3-Formylchromone **1a** has been reduced to the corresponding alcohol **3a** by sodium borohydride in the presence of anhydrous aluminium chloride in tetrahydrofuran (THF) in only 12% yield[2,4]. This poor yield may be attributed to the susceptibility of the pyran 2,3-olefinic bond of 3-formylchromone[5] or the product itself towards this nucleophilic reagent and consequent opening of the pyran ring. So the choice of the reagent for selective reduction of the aldehyde or carboxy function attached to the γ-pyrone ring is rather limited. It is, however, well established that the reactivity of the carboxylic acid group is greater than an olefinic bond towards borane in THF[6]. So for the reduction of the acid **2** to the corresponding alcohol **3**, BH_3-THF complex seemed to be the reagent of choice and it was also of interest to examine how 3-formylchromone **1** would behave towards this reagent. The results obtained by treating the aforementioned chromones **1** and **2** with BH_3-THF complex are presented in this communication.

Stirring of a solution of the aldehyde **1** in THF with excess BH_3-THF complex in THF at ambient temperature under nitrogen atmosphere for an hour followed by decomposition of the reaction mixture with aqueous acetic acid smoothly afforded 3-hydroxymethylchromone **3** in 62-67% yield. Surprisingly, none of the 3-hydroxycarbonylchromones **2** could be reduced under the same conditions; the starting material was recovered nearly quantitatively. No reason for this unusual inertness of the carboxy group and 2,3-olefinic bond of the chromone **2** towards borane can be put forward. It may be mentioned here that the pyrimidine derivative **5** having its carboxy and olefinic functionalities in an electronic environment more or less similar to that in the chromone **2** also eludes reduction by diborane[7].



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Reacting 3-formylchromone **1** with zinc in acetic anhydride followed by acid hydrolysis of the resultant acetate **4** affords the alcohol **3** in approximately 50% yield[8]. The alcohol **3a** has also been prepared in 40% yield by treatment of the acetophenone **6**, derived from salicylic ester and sodium methylsulfinylmethide, with two moles of formaldehyde in the presence of a base and subsequent thermal elimination of MeSOH from the resultant chromone **7**[3]. The Meerwein-Pondorf-Verley type reduction of the aldehyde **1a** at room temperature using 2-propanol over Brockman neutral alumina, activity grade I, in place of Woelem-200-N vacuum dried alumina as prescribed by Posner *et al*[9], *however, yielded the alcohol* **3a** in only 15% yield. Alumina mediated Cannizaro reaction[10] of the aldehyde **1a** attempted by us was also associated with various other transformations of the substrate. So far the synthesis of the target compound **3** is concerned, the method involving reduction of 3-formylchromone **1** by dibroane as revealed in this communication is, however, superior to the above mentioned ones[3,8] because of the improved yield (62-67%) and simple working procedure.

Experimental Section

General procedure for treatment with diborane. A solution of the chromone **1** or **2** (1 mmole) in THF (30-40 mL) was cooled in an ice-bath and continuously purged with nitrogen. The solution was stirred on a magnetic stirrer and to it

†For Part 35 of the series, see ref. 9.

borane-THF complex in THF (1 M, 3ml) added in one lot. The reaction mixture was stirred at 0°C for 10 min and at ambient temperature for 1 hr. The solvent was then evaporated using a rotary evaporator, and the residue treated with aqueous acetic acid (50%, 8 mL) and the mixture again evaporated to dryness. The residue was digested with hot water (8-10 mL) for 5 min and filtered, whereby most of the boric acid formed went into the filtrate. The precipitate was crystallised from methanol-water. Each member of the acid **2** was recovered unchanged in more than 90% yield whereas the aldehyde **1** was reduced to 3-hydroxymethylchromone **3**, the characterisation data of which are given below.

3a : Yield 67%, m.p. 109° (lit.[2]. m.p. 109-10°).

3b : Yield 65%, m.p. 141° (Found : C, 69.5; H, 5.3. $C_{11}H_{10}O_3$ requires C, 69.4; H, 5.5%); IR (KBr): 3350 (OH), 1635 (CO) cm^{-1}; ^1H NMR ($CDCl_3$, 100 MHz) : δ 7.98 (1H, d, J = 2Hz, H-5), 7.92 (1H, s, H-2), 7.48-7.36 (2H, m, H-7,8), 4.58 (2H, s, CH_2), 3.20 (1H, brs, OH) and 2.48 (3H, s, Me).

3c: Yield 62%, m.p. 164° (lit.[3] m.p. 163-64°); ^1H NMR ($CDCl_3$, 200 MHz) : δ 8.17 (1H, d, J = 2.4 Hz, H-5), 7.95 (1H, s, H-2), 7.60 (1H, dd, J = 9, 2.4 Hz, H-7), 7.43 (1H, d, J = 9 Hz, H-8), 4.58 (2H, s, CH_2) and 2.95 (1H, brs, OH); ^{13}C NMR ($CDCl_3$) : δ 177.2 (C-4), 154.9 (C-8a), 153.0 (C-2), 134.2 (C-7), 131.3 (C-6), 125.0 (C-5), 124.7 (C-4a), 123.5 (C-3), 120.0 (C-8) and 58.4 (CH_2).

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